

SUBSTITUTE AMENDMENT AND RESPONSE TO OFFICE ACTION

Amendment

In the Claims

Claims 1-15 (canceled).

16. (currently amended) Dry microparticles having a size range of between 0.5 and ten microns comprising a drug to be delivered by inhalation, wherein the microparticles are formed of a material releasing drug at a pH of ~~greater than 6.0~~ or greater, wherein the material is selected from the group consisting of alginate, chitosan, hydrophilic or hydrophobic proteins, polymers of mixed amino acids, polysaccharides, and lipids and surface active agents.

17. (canceled)

18. (currently amended) The dry ~~microparticle~~ microparticles of claim 16 wherein the material is a lipid.

19. (currently amended) The dry ~~microparticle~~ microparticles of claim 16 wherein the proteins are hydrophilic proteins.

20. (currently amended) The dry ~~microparticle~~ microparticles of claim 16 wherein the proteins are hydrophobic proteins.

21. (canceled)

22. (currently amended) A cartridge for insertion into an inhaler comprising dry microparticles having a size range of between 0.5 and ten microns comprising a drug to be delivered by inhalation, wherein the microparticles are formed of a material releasing drug at a pH of ~~greater than 6.0~~ or greater, wherein the material is selected from the group consisting of

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alginate, chitosan, hydrophilic or hydrophobic proteins, mixed amino acids, polysaccharides, and lipids and surface active agents.

23. (currently amended) A method for delivery of ~~microparticles~~ an active agent to the pulmonary system comprising: administering to a patient in need of treatment an effective amount of microparticles which comprise a diketopiperazine and ~~an~~ the active agent and which have a diameter between 0.5 microns and ten microns, in a pharmaceutically acceptable carrier for administration to the lungs, wherein the carrier is air, wherein the microparticles are administered from a dry powder inhaler or from a container for a dry powder inhaler, and wherein the active agent is released from the microparticle at a pH of ~~greater than 6.0~~ or greater.

24. (previously presented) The method of claim 23, wherein the diketopiperazine has the formula 2, 5 --diketo-3,6-di(4-X-aminobutyl)piperazine, wherein X is selected from the group consisting of succinyl, glutaryl, maleyl, and fumaryl.

25. (previously presented) The method of claim 24, wherein X is fumaryl.

26. (previously presented) The method of claim 23, wherein the agent is a therapeutic agent selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

27. (currently amended) A microparticulate system for ~~controlled~~ drug delivery to the pulmonary system comprising: microparticles incorporating therein a therapeutic, prophylactic or

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diagnostic agent, wherein the microparticles have a diameter between 0.5 microns and ten microns and are formulated to release the incorporated agent at a pH of 6.0 or greater ~~under~~ conditions ~~present in the pulmonary system~~, in a pharmaceutically acceptable carrier for administration to the lungs, wherein the carrier is air, wherein the microparticles are in a dry powder inhaler or a container for a dry powder inhaler, and wherein the microparticles ~~are made from~~ consist essentially of the therapeutic, prophylactic or diagnostic agent and a material selected from the group consisting of ~~diketopiperazines~~, poly(hydroxy acids), polyanhydrides, polyesters, polyamides, polycarbonates, polyalkylenes, polyvinyl compounds, polysiloxanes, polymers of acrylic and methacrylic acids, polyurethanes and co-polymers thereof, ~~poly(butic acid)~~ poly(butyric acid), poly(valeric acid), poly(lactide-co-caprolactone), polysaccharides, and copolymers and mixtures thereof.

Claims 28-30. (canceled)

31. (previously presented) The system of claim 27, wherein the agent is a therapeutic agent selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

32. (currently amended) A method for ~~controlled~~ drug delivery to the pulmonary system comprising: administering to a patient in need of treatment an effective amount of microparticles incorporating therein a therapeutic, prophylactic or diagnostic agent, wherein the microparticles

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have a diameter between 0.5 microns and ten microns and are formulated to release the incorporated agent at a pH of 6.0 or greater ~~under conditions present in the pulmonary system~~, in a pharmaceutically acceptable carrier for administration to the lungs, wherein the carrier is air, wherein the microparticles are administered from a dry powder inhaler or from a container for a dry powder inhaler, and wherein the microparticles ~~are made from~~ consist essentially of the therapeutic, prophylactic or diagnostic agent and a material selected from the group consisting of diketopiperazines, poly(hydroxy acids), polyanhydrides, polyesters, polyamides, polycarbonates, polyalkylenes, polyvinyl compounds, polysiloxanes, polymers of acrylic and methacrylic acids, polyurethanes and co-polymers thereof, ~~poly(butic acid)~~ poly(butyric acid), poly(valeric acid), poly(lactide-co-caprolactone), polysaccharides, and copolymers and mixtures thereof.

Claims 33 - 35. (canceled)

36. (previously presented) The method of claim 32, wherein the agent is a therapeutic agent selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

37. (new) The cartridge of claim 22, wherein the cartridge is suitable for use in a dry powder inhaler.

38. (new) A method for delivery of a drug to the pulmonary system comprising: administering to a patient in need of treatment an effective amount of microparticles comprising

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the drug, wherein the microparticles have a diameter between 0.5 microns and ten microns, wherein the microparticles are formed of a material releasing drug at a pH of 6.0 or greater, wherein the material is selected from the group consisting of alginate, chitosan, hydrophilic or hydrophobic proteins, and lipids, in a pharmaceutically acceptable carrier for administration to the lungs, wherein the carrier is air.

39. (new) The method of claim 38, wherein the drug is selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

40. (new) A microparticulate system for drug delivery to the pulmonary system comprising microparticles having a size range of between 0.5 and ten microns, wherein the microparticles comprise an effective amount of a drug to be delivered and a diketopiperazine, and wherein the microparticles release the drug at a pH of 6.0 or greater, in a pharmaceutically acceptable carrier for administration to the lungs, wherein the carrier is air, and wherein the microparticles are in a dry powder inhaler or a container for a dry powder inhaler.

41. (new) The system of claim 40, consisting essentially of the drug and the diketopiperazine.

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42. (new) The system of claim 40, wherein the diketopiperazine has the formula 2, 5 – diketo-3,6-di(4-X-aminobutyl)piperazine, wherein X is selected from the group consisting of succinyl, glutaryl, maleyl, and fumaryl.

43. (new) The system of claim 42, wherein X is fumaryl.

44. (new) The system of claim 40, wherein the drug is selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

45. (new) The system of claim 44, wherein the drug is insulin.

46. (new) The method of claim 26, wherein the drug is insulin.

47. (new) A cartridge for insertion into an inhaler comprising dry microparticles having a size range of between 0.5 and ten microns comprising a drug to be delivered by inhalation, wherein the microparticles comprise a diketopiperazine and the drug, and wherein the microparticles release the drug at a pH of 6.0 or greater.

48. (new) The cartridge of claim 47, wherein the drug is selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

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49. (new) The cartridge of claim 48, wherein the drug is insulin.

50. (new) A cartridge for insertion into an inhaler comprising dry microparticles having a size range of between 0.5 and ten microns comprising a drug to be delivered by inhalation, wherein the microparticles consist essentially of the drug and a material selected from the group consisting of poly(hydroxy acids), polyanhydrides, polyesters, polyamides, polycarbonates, polyalkylenes, polyvinyl compounds, polysiloxanes, polymers of acrylic and methacrylic acids, polyurethanes and co-polymers thereof, poly(butyric acid), poly(valeric acid), poly(lactide-co-caprolactone), polysaccharides, and copolymers and mixtures thereof, and wherein the microparticles release the drug at a pH of 6.0 or greater.

51. (new) The cartridge of claim 50, wherein the drug is selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

52. (new) The microparticles of claim 16, wherein the drug is selected from the group consisting of insulin, calcitonin, felbamate, heparin, parathyroid hormone and fragments thereof, growth hormone, erythropoietin, zidovudine (AZT), didanosine (DDI), granulocyte colony stimulating factor (G-CSF), lamotrigine, chorionic gonadotropin releasing factor, luteinizing releasing hormone, β -galactosidase, and Argatroban.

53. (new) The microparticles of claim 52, wherein the drug is insulin.

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54. (new) The microparticles of claim 18, wherein the drug is insulin.